## REMARKS/ARGUMENTS

Claims 1, 3-5, 9-22, 25-40, 78, and 79 are pending and stand substantively rejected. Claims 1, 4, 18, 19, 78, and 79 are presently amended, and claim 80 is added. The paragraph headings below follow that of the Office Action.

**1. Claim Amendments and New Claim**

Amended claims 1, 78, and 79, and new claim 80 recite treatment with a taxane, which is a microtubule affecting agent. Microtubule affecting agents are discussed in the specification (e.g. p. 19, line 28 to page 20, line 4), and some of the references mentioned there further discuss taxanes (e.g. U.S. Patent No. 5,530,020). This patent is incorporated by reference in the specification (e.g. p. 89, lines 20-21). Thus, recitation of the term "taxane" does not introduce new matter. New claim 80 recites treatment of cancer cells that includes contacting a sample of the cancer cells with certain agents. Such procedures are described in the specification (e.g. p. 39, lines 20-22), and do not represent new matter.

**2. Declaration**

The Action states that the Declaration is defective because the priority information on the signed Declaration does not match the priority claimed in the first line of the Specification.

According to MPEP 602.05(a), a continuation application may be filed with a copy of the Declaration from the prior nonprovisional application.

A. The Declaration

The present application is a continuation of U.S. Patent Application No. 09/024,932. A copy of the Declaration from the parent was filed in the instant application. The Declaration indicates that U.S. Patent Application No. 09/024,932 claims the benefit of priority of U.S. Patent Application Nos. 60/038,065 and 60/047,834.

B. The Specification

On or about March 12, 2004, Applicant filed a Preliminary Amendment which amended the priority data in the instant Specification. As amended, the Specification indicates the following:

> *"The present application is a continuation of Application No. 09/024,932, filed February 17, 1998, which claims priority from U.S. Provisional Application No. 60/038,065, filed February 18, 1997, now abandoned; and, U.S. Provisional Application No. 60/047,834, filed May 28, 1997, now abandoned."*

Based on the above, Applicant submits that the priority data on the signed Declaration does match the priority claimed in the Specification. Withdrawal of this Objection is respectfully requested.

**3. Election/Restrictions**

Applicant acknowledges that renumbered Restriction Group II (previously Groups. II, IV, and VI) is presently under consideration.

**4. Claim Objections**

Claim 18 is objected to because the trademark TAXOTERE® is not capitalized. Claim 18 is presently amended to recite "docetaxel" instead of TAXOTERE®. Docetaxel is the generic terminology for TAXOTERE®. Similarly, claim 19 is presently amended to recite "paclitaxel" instead of TAXOL®. Paclitaxel is the generic terminology for TAXOL®.

**5. First Rejection Under 35 U.S.C. §112**

Claims 1, 3-5, 9-22, 25-40, 78, and 79 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. This rejection is traversed.

A. Treatment Environment

The Office Action (pp. 4-5 and 13-14) states that the specification is enabling only for *in vitro* and *in vivo* treatment environments. Applicant disagrees. According to MPEP 2164.08, enablement requires that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. In addition to the *in vitro* methods

that are acknowledged as enabled, Applicant submits that a broad range of *in vivo* and *ex vivo* treatment environments were known to the artisan at the time the instant application was filed.

For example, Nielsen et al., in "p53 Tumor Suppressor Gene Therapy for Cancer," *Cancer Gene Therapy* 5(1):52-63 (1998) ["Nielsen I"] (copy enclosed), catalog several examples of efficacious *in vivo* and *ex vivo* treatment environments for p53 gene therapy (e.g. Table 3 at pp. 58-59). Clearly, at the time the present application was filed, p53 gene therapy in various treatment environments were known to the artisan. In this regard, the presently pending claims are fully enabled by the teachings of Applicant's specification.

B. Mode of Delivery

The Office Action (pp. 4-5 and 13-14) states that in the case of the *in vivo* treatment environment, the specification is enabling for only one mode of delivery: intratumoral injection. Applicant disagrees. Again, referring to Table 3 of Nielsen I, a broad range of efficacious modes of delivery for p53 gene therapy are noted, including intra-/peritumoral, intravenous, intraperitoneal, intratracheal, intrahepatic artery, and hepatic portal vein modes of delivery. Thus, at the time the present application was filed, p53 gene therapy via various modes of administration were known to the artisan. In this regard, the presently pending claims are fully enabled by the teachings of Applicant's specification.

To further confirm enablement, Applicant encloses a copy of Nielsen et al., "*Adenovirus-mediated p53 Gene Therapy and Paclitaxel Have Synergistic Efficacy in Models of Human Head and Neck, Ovarian, Prostate, and Breast Cancer*," Clin. Cancer Research 4:835-846 (1998) ["Nielsen II"], which illustrates that the artisan would be enabled by the instant application to practice the presently claimed invention.

It is also noted that currently pending claim 79 is drawn to the *in vitro* method which the Office Action indicates *is* enabled. Based on the foregoing, withdrawal of this rejection is respectfully requested.

C. Other Treatment Parameters

Although there is some discussion that the present claims read broadly on treatment of any cancer from any organism with any tumor suppressor nucleic acid (Office Action at p. 6) and that the specification does not teach certain vector methods (Office Action at

pp. 7-10), antisense techniques (Office Action at pp. 10-11), or human therapies (Office Action at pp. 12-13), the claims do not appear to be rejected on this basis according to what the Office Action states *is* enabled (Office Action at pp. 4-5 and 13-14). If the Office Action was intended to include these other treatment parameters as part of the enablement rejection, Applicant respectfully requests clarification.

**6. Second Rejection Under 35 U.S.C. §112**

Claims 1, 3-5, 9-22, and 25-40 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. This rejection is overcome in part and traversed in part as follows.

Claim 1 is amended as suggested by the Office Action to recite "contacting said cancer cells." Claim 4 is amended to recite "the cells." No new matter is introduced by these amendments. The related dependent claims are now definite in this regard. A similar amendment is made to claim 79.

Claim 3 is rejected because the term "paclitaxel derivative" is allegedly indefinite. Applicant submits that this term is discussed in the specification at p. 19, line 28 to page 20, line 4, and would be well understood by the artisan. However, if other issues in the Office Action can be resolved, Applicant may consider amending this claimed element.

**7. Rejection Under 35 U.S.C. §102**

Claims 1, 3, 9, 10, 20, and 79 were rejected under 35 U.S.C. 102(b) as allegedly anticipated by Blagosklonny et al., Int. J. Cancer, 67:386-392 (1996) ["Blagosklonny"]. This rejection is overcome as follows.

According to MPEP 2131, to anticipate a claim, a reference must teach every element of the claim. Amended independent claims 1 and 79 are drawn to methods that include, *inter alia*, contacting cells with a nucleic acid encoding p53 and with a taxane. Blagosklonny discusses treatment with a nucleic acid encoding p53 and with mitomycin C, Adriamycin, or vincristine, none of which are a taxane. Because Blagosklonny does not disclose treatment with a taxane (e.g. paclitaxel), this reference does not teach every claimed element and therefore is not anticipatory. Claims 3, 9, 10, and 20 depend either directly or indirectly from claim 1, and

therefore are allowable because they depend on an allowable base claim, as well as for the novel combination of elements they recited. Withdrawal of this rejection is respectfully requested.

**8. Rejection Under 35 U.S.C. §103**

Claims 1, 3-5, 9-22, 25-40, 78, and 79 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Kalechman et al., J. Immunol., 156:1101-1109 (1996) ["Kalechman"], in view of Gallardo et al., Cancer Res., 56:4891-4893 (1996) ["Gallardo"] or Fujiwara et al., Cancer Res., 54:2287-2291 (1994), further in view of Mujoo et al., Oncogene, 12:1617-1623 (1996) ["Mujoo"]. This rejection is respectfully traversed, particularly as applied to the claims as amended.

According to MPEP 2142, to establish a *prima facie* case of obviousness, (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to the artisan, to modify the reference or to combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the cited reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the cited references, and not based on applicant's disclosure.

As noted by the Examiner, Kalechman discusses treatment of lung cancer cells with paclitaxel, but does not teach contacting the cells with a nucleic acid encoding p53. Gallardo discusses treatment of ovarian cancer cells with a nucleic acid encoding p53, but fails to teach or suggest contacting the cells with a taxane. Fujiwara discusses treatment of lung cancer cells with a nucleic acid encoding p53, but fails to teach or suggest contacting the cells with a taxane. Mujoo discusses treatment of ovarian cancer cells with a nucleic acid encoding p53, but fails to teach or suggest contacting the cells with a taxane.

As Applicant understands it, the Office Action asserts that it would be obvious to combine a p53 treatment with a paclitaxel treatment because even if the effects are additive, using two treatment methods would be better than one treatment method. Applicant disagrees.

The law is clear on this point. It is well settled that non-obviousness can be established by a showing of evidence that the claimed invention yields surprising or unexpectedly improved properties. [MPEP § 2144.08(II)(B)] A greater than expected result is

an evidentiary factor pertinent to the legal conclusion of obviousness, and may be shown by demonstrating an effect which is greater than the sum of each of the effects taken separately (i.e., demonstrating "synergism"). [Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989)]

Unexpected results are demonstrated by Nielsen II who report a synergistic effect of the combination of p53 and a taxane (e.g. paclitaxel) in four cell lines: human head and neck, ovarian, prostate, and breast cancer cells (e.g. Table 1, p. 837).. This is objective evidence that treatment with p53 and a taxane has a surprising and unexpected effect in these human cancer cells.

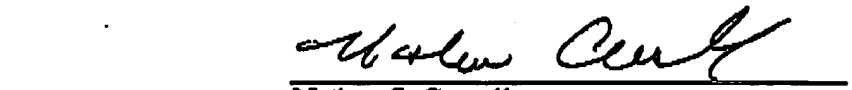
The record demonstrates that the substantially improved properties of treatment with p53 and a taxane are unexpected and would not have been obvious. Absent a showing that the results provided in Nielsen II would have been expected by the artisan, the rejection under §103 must be withdrawn.

## CONCLUSION

In view of the foregoing, Applicant believes all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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